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(54) Title: BONE IMPLANT

(57) Abstract

The invention concerns an implant for guided or controlled bone tissue regeneration. The implant consists essentially of a three-dimensional material having a form that allows bone cells to attach to it or can be modified to allow cells to attach to it and which allows cells to grow in more than one layer. According to the invention, the material essentially consists of a biocompatible, fibrous material.

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BONE IMPLANT

The present invention concerns an implant for guided or controlled bone tissue regeneration.

Guided tissue regeneration is a known technique for creating new periodontal attachment to real teeth. This technique is based on the assumption that only some of the cell types in the jaw have a positive effect on the creation of supporting tissue, whereas other types have a negative effect. The latter, i.e. the epithelium, connective tissue and bone cells, should be prevented from reaching the tooth, whereas the former, mostly from the periodontal ligament, should have free access thereto. To keep away the undesired cells, "cell-tight" filters or membranes placed near the tooth are used. The membrane, which is soft, is applied or applies itself to the tooth. A much-used membrane consists of expanded PTFE and is sold under the tradename of GORE periodontal membrane (Gottlow et al J. Clin. Periodontology 1984; 9: 494-503; Pontoriero, R. et al J. Clin. Periodontology 1988; 15: 247-254; Pontoriero, R. et al J. Clin Periodontology 1989; 16: 170-174; Gottlow, J. et al 1986; 13: 604-616; Becker, W. et al Int. J. Periodont. Rest. Dent. 1988; 3: 2-16).

When modified, this technique is said to be useful in connection with fixtures. The flat membrane is applied to the top of the fixture, under the flap (Dahlin et al Int. J. Oral Maxillofac. Implants 1989; 4(1): 19-25; Becker, W. et al Int. J. Periodont. Rest. Dent.. 1990; 10: 93-102). However,it has been found that this technique gives no satisfactory regeneration of bone tissue.

As disclosed in the patent publication PCT/SE91/00216 it has however been found that soft, cell-tight membranes are not suitable for recreating bone tissue in connection with fixtures, i.e. coronally of (above) the surrounding bone level. Instead it was found

that cells in the jaw that previously were considered disadvantageous in the recreation of bone tissue are actually extremely advantageous in this process. Therefore bone cells from the periosteum and the bone edge should be given access to the operation area round the fixture. This accessibility can be created by the rigidity and the perforations of the device according to this patent publication.

This technique is also disclosed in an article by S. Jovanovic et al in Volume 10, No. 1, 1995 of The International Journal of Oral and Maxillofacial Implants. According to this article, supracrestal bone formation was demonstrated by a submerged membrane therapy in a dog model. The bone formation was obtained by using reinforced e-PTFE membranes with titanium. These membranes preserved their original form during the investigation, provided a large space for blood-clot stabilisation and resulted in more bone when compared to the use of standard membranes.

It has now been found that sufficient rigidity and space-providing ability can be obtained if the mesh used according to the article by Jovanovic et al is replaced by a fibrous material, preferably in the form of wool.

The publication WO 9007308 discloses a barrier which could be in the form of a fibrous material. The barrier is intended for regeneration of bone supporting tissue and is said to give a predictable healing sequence including a regeneration of firstly, periodontal ligament tissue, secondly, surrounding alveolar bone tissue and, thirdly, gingival connective tissue and epithelium. It is critical that the barrier is used in combination with a separating means including e.g. protuberances. Furthermore, it is recommended that the barrier should consist of a biodegradable material.

In contrast to this known material which should give a specific healing sequence of different cells, the fibrous material according to the present invention is

intended for use as an implant for guided or controlled regeneration or growth of primarily or essentially only bone cells in surgically intervened areas. No separating means of the kind necessary according to the patent publication WO 9007308 is required. Furthermore, according to the present invention, the guided growth or regeneration of the bone cells is determined by the shape and the material of the implant and depends on the damage to be remedied. In practice the shape of the implant is determined by the person performing the surgery.

The new implant according to the present invention essentially consists of a three-dimensional, space-creating, porous, biocompatible, non-biodegradable material having a form that allows bone cells to attach to it or which can be modified to allow cells to attach to it and which allows cells to grow three-dimensionally. It is critical that the material is fibrous, and preferably in the form of wool. Especially preferred forms are wool strings or pads, which can easily be tailored to the desired form by the surgeon.

The new material according to the invention should have a sufficient strength to withstand the pressure prevailing in the region of the body where it is to be inserted and it should also have a suitable porosity.

The actual diameter of the fibre may vary depending on the site in body and the required strength. Normally this diameter will be less than 1 mm, preferably less than 0.5 mm and most preferably less than 0.1 mm.

As regards the porosity it is obvious that the more porosity the more the bone cells will be formed within the space of the implant. If, however, the porosity is too large the ability of the implant to withstand pressure exerted by the adjacent tissues will decrease. If, on the other hand, drilling operations are to be expected, e.g. for the fixation of screws, in the newly created bone, the porosity should not be too low. The optimal porosity will therefore depend on the place where

the fibrous material is to be used and is easily determined by the person skilled in the art.

The new biocompatible implant preferably consists of titanium or titanium-coated fibres. Preferably the fibres are in the form of titanium wool. Other types of material are ceramic materials.. Furthermore the new material can be provided in the form of strings or pads, which optionally can be at least partially covered by a film or membrane of e.g. polylactic acid in order to avoid optional fibre penetration through the mucous membranes.

In comparison with the devices known from the PCT/SE91/00216 publication and the above article by Jovanovic et al, the device according to the present invention confers several advantages. Thus the new device can be obtained in almost any shape and more or less tailored for the intended use. The new material also provides an increased surface for rapid bone regeneration, as it has been proved that newly formed bone cells have a tendency to climb on a surface, thereby increasing the proliferation of the bone cells. Another advantage is that the device can be manufactured without expensive production equipment. Other advantages concern the possibility of coupling bone morphogenic proteins (BMPs) to fibres according to the invention.

The new device can also be useful in areas other than teeth prosthetics, where there are problems with replacing parts of the skeleton that have lost their original shape. After a traffic accident, crushed or caved-in skeleton parts of the face may have to be replaced, and in bone neoplasm therapy, it is sometimes necessary to surgically remove skeleton parts which may need to be replaced.

The method of using the implant can be described as follows:

The area in which the implant is to be installed is first uncovered by raising one or two separate

mucoperiostal flaps. Minor perforations (0.5-1 mm in diameter) are done in the bone tissue in order to perforate the compact bone wall and facilitate bleeding into the wound area. This technique improves the bone regeneration procedure in the area to be regenerated. The area is inspected by the surgeon and a proper implant size is chosen. The implant will thereafter be trimmed in order to fit the defect morphology. The implant is, if necessary, fixated to the bone. For example, small screws could do this in different ways. The soft tissues are trimmed and placed over the implant in such a way that this is completely covered by the flaps. The flaps are sutured and the area is left for healing. During the healing phase the area should be protected from external forces. This means that if the implant is used in the mouth, removable dentures should not be worn during the phase of healing.

CLAIMS

1. A new implant essentially consisting of a three-dimensional, essentially non-biodegradable, space-creating, porous, biocompatible material having a form that allows bone cells to attach to it or which can be modified to allow such cells to attach to it and which allows primarily bone cells to grow three-dimensionally, c h a r a c t e r i s e d in that the implant essentially consists of a fibrous material.

2. The implant according to claim 1, c h a r a c t e r i s e d in that the fibrous material essentially consists of titanium or titanium-coated fibres.

3. The implant according to claim 1, c h a r a c t e r i s e d in that it is at least partially covered by a bioresorbable membrane.

4. The implant according to any one of the preceding claims, c h a r a c t e r i s e d in that it is in the form of titanium wool strings or pads.

5. The implant according to any one of the preceding claims, c h a r a c t e r i s e d in that it also includes bone morphogenic factors.

6. Use of an implant which allows primarily bone cells to grow three-dimensionally and which essentially consists of a three-dimensional, essentially non-biodegradable, space-creating, porous, biocompatible material having a form that allows bone cells to attach to it or which can be modified to allow such cells to attach to it and which essentially consists of a fibrous material.

7. Method of providing selective bone tissue regeneration or growth, c h a r a c e r t i s e d in that a defined space for bone tissue growth is provided by surgical intervention, that an implant essentially consisting of a three-dimensional, essentially non-biodegradable, space-creating, porous, biocompatible

material having a form that allows bone cells to attach to it or which can be modified to allow such cells to attach to it and which essentially consists of a fibrous material, is arranged in the selected implant area, and that soft tissues are trimmed and replaced over the implant in such a way that the soft tissue after suturing completely covers the implant.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 98/00265

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61C 8/00, A61F 2/28, A61L 27/00
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61C, A61F, A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 9007308 A1 (PROCORDIA ORATECH AB), 12 July 1990 (12.07.90), page 10, line 7 - line 19, claims 1-15	1-5
A	US 3867728 A (JAMES A. STUBSTAD ET AL), 25 February 1975 (25.02.75), column 5, line 29 - line 47, abstract	1-5
A	WO 9114404 A1 (TITANBRON I ÅHUS AB), 3 October 1991 (03.10.91), page 5, line 8 - line 11	1-5

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 May 1998	20-05-1998
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Jack Hedlund Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 98/00265

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 6-7
because they relate to subject matter not required to be searched by this Authority, namely:
See PCT Rule 39.1(iv): Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

29/04/98

International application No.
PCT/SE 98/00265

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9007308 A1	12/07/90	DE 68913556 D,T	25/08/94
		DK 122091 A	21/06/91
		DK 171525 B	23/12/96
		EP 0449941 A,B	09/10/91
		SE 0449941 T3	
		ES 2049971 T	01/05/94
		JP 3505684 T	12/12/91
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		NO 177035 B,C	03/04/95
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